Supplementary Online Content

Franceschini N, Kopp JB, Barac A, et al. Association of *APOL1* with heart failure with preserved ejection fraction in postmenopausal African American women. *JAMA Cardiol.* Published online July 3, 2018. doi:10.1001/jamacardio.2018.1827

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Baseline characteristics of individuals developing heart failure, by heart failure subtype

Characteristics	Unclassified heart failure (n=95)	HFpEF (n=154)	HFrEF (n=144)
Age, mean (SD), years	65.8 (7.7)	64.9 (7.1)	63.8 (7.5)
Education, < high school, No. (%)	13 (13.7)	23 (14.9)	41 (18.8)
Ever smoker, No. (%)	52 (54.7)	88 (57.1)	77 (53.5)
Overweight/obese, No. (%)	17 (17.9)/69 (72.6)	38 (24.8)/108 (70.6)	50 (36.0)/70 (50.4)
Diabetes, No. (%)	21 (22.1)	49 (31.8)	41 (28.5)
Hypertension, No. (%)	78 (82.1)	121 (78.6)	113 (78.5)
History of cardiovascular disease, No. (%)	42 (44.2)	55 (36.2)	59 (41.6)
eGFR, mean (SD), ml/min/1.73 m^2	84.3 (23.9)	82.8 (23.4)	86.3 (23.9)
CKD, No. (%)	15 (15.8)	28 (18.2)	20 (13.9)
APOL1 high risk/low risk, No. (%)	10 (10.5)	26 (16.8)	18 (12.5)

Three participants who recovered ejection fraction acute decompensated heart failure are not included in the subtype classification.

eTable 2. Association of *APOL1* with ESRD and cardiovascular outcomes in a subsample with genome-wide association data

Incident outcomes	Total No.	No. Events	*Model 1*	*Model 2*	*Model 3*
		APOL1 low /high risk	HR (95% CI)	HR (95% CI)	HR (95% CI)
ESRD	7,819	153/29	1.28 (0.84, 1.93)	1.26 (0.83, 1.90)	0.89 (0.58,1.37)
CHD[a]	6,217	463/67	1.15 (0.89, 1.49)	1.20 (0.93, 1.56)	1.19 (0.92, 1.55)
All-cause stroke	7,819	398/49	0.90 (0.67, 1.21)	0.83 (0.66, 1.21)	0.86 (0.64, 1.16)
Ischemic stroke	7,819	279/30	0.78 (0.54, 1.14)	0.79 (0.54, 1.15)	0.76 (0.52, 1.12)
All-cause heart failure	7,797	302/50	1.27 (0.94, 1.71)	1.24 (0.91, 1.67)	1.19 (0.88, 1.61)
HFpEF[b]	7,672	117/25	1.69 (1.10, 2.61)	1.61 (1.04, 2.50)	1.55 (0.997, 2.40)
HFrEF[b]	7,655	108/17	1.19 (0.71, 1.98)	1.16 (0.69, 1.94)	1.13 (0.67, 1.89)
All-cause death	7,819	1,430/194	1.04 (0.90, 1.21)	1.02 (0.87, 1.18)	0.99 (0.85, 1.16)
Cardiovascular death	7,819	514/75	1.10 (0.86, 1.40)	1.06 (0.83, 1.35)	1.03 (0.80, 1.31)
Composite CHD/stroke[a]	6,217	621/83	1.03 (0.82, 1.30)	1.06 (0.84, 1.33)	1.04 (0.83, 1.32)

[a] exclusion of prevalent cases. [b] unclassified heart failure events were excluded.

Model 1: Adjusted for age, waist, education, income, region, smoking, systolic and diastolic blood pressures, hypertension treatment, diabetes, enrolled in OS vs CT, and use of lipid medications. Model 2, Model 1 and further adjusted for the first three principal components of ancestry. Model 3: Model 2 further adjusted for baseline glomerular filtration rate.

eTable 3. Association of *APOL1* with cardiovascular disease outcomes using number of copies of *APOL1* risk status.

Incident outcomes			
	HR (95% CI)	*p* for trend	
CHD	1.04 (0.92, 1.18)	0.51	
All-cause stroke	0.98 (0.86, 1.11)	0.73	
Ischemic stroke	0.97 (0.83, 1.13)	0.66	
All-cause heart failure	1.00 (0.87, 1.17)	0.96	
HFpEF	1.13 (0.90, 1.44)	0.30	
HFrEF	0.97 (0.76, 1.24)	0.80	
All-cause death	1.03 (0.96, 1.10)	0.46	
Cardiovascular death	1.03 (0.92, 1.16)	0.59	
Composite CHD and ischemic stroke	1.03 (0.93, 1.14)	0.63	

Additive genetic models using *APOL1* risk categories of zero, 1 and 2 copies of risk genotypes, adjusted for age, waist, education, income, region, smoking, systolic and diastolic blood pressures, hypertension treatment, diabetes, enrolled in OS vs CT, and use of lipid medications. HR, hazard ratio; CI, confidence interval

eTable 4. Estimated power for two-sample comparison of survivor functions, using a two-sided test and alpha=0.05.

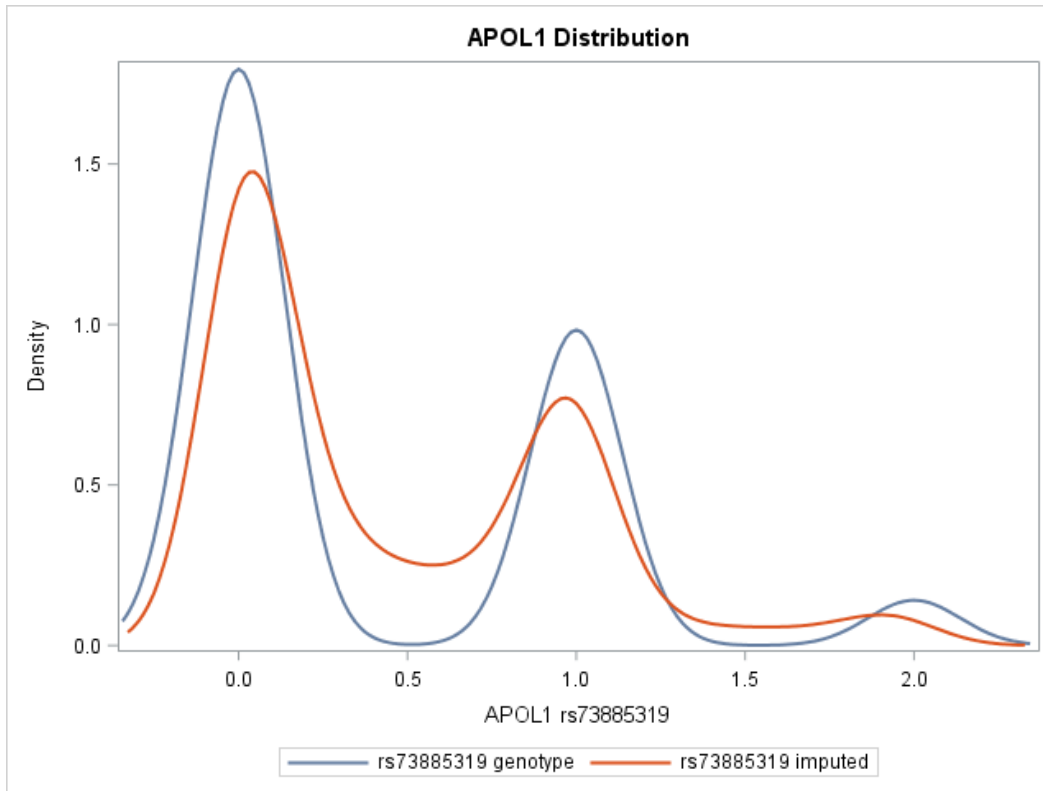| Sample=11,137	Control/cases ratio (N2/N1)							
Hazard ratio	5	10	20	30	40	50	60	70
1.1	0.96	0.81	0.54	0.39	0.30	0.25	0.21	0.18
1.2	1.00	0.99	0.98	0.92	0.82	0.72	0.63	0.55
1.3	1.00	1.00	1.00	0.99	0.99	0.97	0.93	0.88
1.4	1.00	1.00	1.00	1.00	0.99	0.99	1.00	0.99
1.5	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Sample=7,796								
1.1	0.87	0.65	0.40	0.28	0.22	0.18	0.15	0.13
1.2	1.00	1.00	0.92	0.78	0.65	0.54	0.46	0.39
1.3	1.00	1.00	1.00	0.98	0.94	0.87	0.79	0.71
1.4	1.00	1.00	1.00	1.00	0.99	0.98	0.96	0.92
1.5	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.99

In red, power above 80%.

For sample n=11,137: N2/N1 ratio CHD=18, all-cause stroke=20, ischemic stroke=29, all-cause heart failure=27, HFpEF=71, HFrEF=76, all-cause death=5, cardiovascular death=17.
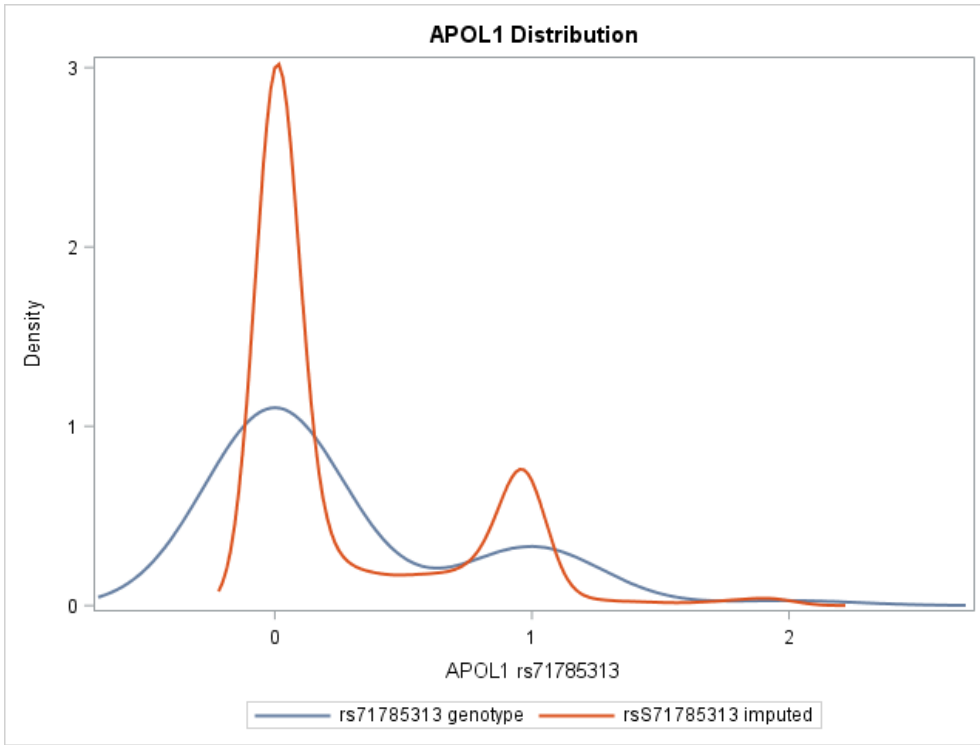
For sample n=7,796: N2/N1 ratio CHD=16, all-cause stroke=24, ischemic stroke=21, all-cause heart failure=54, HFpEF=61, HFrEF=4, all-cause death=12, cardiovascular death=10.

eFigure 1. Correlation of imputed and genotype variants and *APOL1* risk groups. Graphs showed the kernel density estimates by subgroups. Note that genotypes are coded 0, 1 or 2 copies but imputed data is a continuous number between 0 and 2. Figure 1A. G1 allele (rs73885319), Figure 1B. G2 allele (rs71785313), Figure 1C. Combined G1/G2 alleles: 0 risk alleles (G0/G0), 1 risk allele (G1/G0, G2/G0), 2 risk alleles (G1/G1, G2/G2, G1/G2).

A

APOL1 Distribution

B

APOL1 Distribution

C

APOL1 Distribution